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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,296	06/21/2001	Thomas E. Tarara	0054.10	6348

21968 7590 07/21/2003

NEKTAR THERAPEUTICS
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EXAMINER
GOLLAMUDI, SHARMILA S

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/21/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/886,296	Applicant(s) TARARA ET AL.	
	Examiner Sharmila S. Gollamudi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-15,18-23,39-47 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-15,18-23,39-47 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachm nt(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Extension of Time, Request for Continued Examination, Amendment D, and Information Disclosure Statement received on May 13, 2003 is acknowledged. Claims 4-15, 18-23, 39-47, and 49-51 are included in the prosecution of this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 recites the limitation of an active agent. This is unclear since the independent claim which it depends form already includes an active agent. Further clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4, 8-15, 18-23, 39-47, and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913, cited prior art) in view of Cohen et al (5149543) by themselves, or in further view of Yen (5308620, cited prior art).

Hanes et al teach aerodynamically light particles for drug delivery to the pulmonary system. The particles have a tap density of less than 0.4 g/cm3 and a diameter between 5 to 30 microns (Note abstract). Hanes teaches features such as irregular surface texture and porous structure contribute to low tap density and manipulation of these features permits the delivery of larger particle envelope volumes into the lungs (col. 9, lines 10-25). Further, low tap density particles are taught to have small aerodynamic diameter (instant diameter) (col. 9, lines 26-45). The particles contain surfactants such as DPPC (instant gel to liquid temperature) and the microstructures are taught to encapsulate active agents, which allows the active to remain protected (col. 10, lines 37-50 and examples). Polylactic acid, polymers of acrylic acids and methacrylic acids may be used to make the microsphere. Further, the particles may be formed into microspheres by methods such as coacervation, interfacial polymerization, etc. (note col. 6). Instant therapeutic agents are taught on column 10, lines 4-30.

Hanes et al do not teach the use of calcium in the structural matrix.

Cohen et al teach a method of making microspheres. The method is based on the use of water-soluble polymers with charged sides that are crosslinked with multivalent cations (abstract). Suitable polymers that are reacted with cations are polyacrylic acids, polymethacrylic acid, PCPP, etc (col. 4, lines 1-5). The cations taught are calcium, copper, magnesium, etc (col. 6, line 22).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hanes and Cohen since Cohen teaches the method of making microspheres thorough coacervation using cations such as calcium. One would be motivated to do so with the expectation of similar results since Hanes teaches the use of polymers with charged sides such as polyacrylic acids, etc. and teaches that any process of making the microsphere is suitable.

The manipulation of tap density and pore size are deemed obvious to one of ordinary skill in the art since Hanes teaches the manipulation of surface roughness (porosity), diameter, and tap density determine the delivery site of the particles (col. 8, lines 19-68). Therefore, one would be motivated to manipulate the factors and fabricate the microstructure according to the region to be targeted.

Response to Arguments

Applicant argues that there is not motivation for one of ordinary skill in the art to combine the references in the manner set forth. Applicant argues that the claims recite a phospholipid structural matrix and zwitterionic. Therefore, it is argued that a skilled artisan would not be motivated to combine the cationic cross-linking agents of Cohen et al with phospholipids are not similar to the gel forming materials of Cohen et al.

Applicant's arguments have been fully considered but they are not persuasive. First, the examiner points out that the claims recite a structural matrix that comprises an active agent, calcium, and a phospholipid; however the claims do not recite a phospholipid structural matrix as argued by applicant. Furthermore the structural matrix can include other polymers since the claim language allows for the matrix to include other componenets. The examiner points to column 6, lines 1-40 Hanes et al teach that the particles are made from various biodegradable material such as polymers of acrylic and methacrylic acids. Cohen et al teach a method of making microcapsules by crosslinking polymers, such as those taught in Hanes et al on column 6, with multivalent ions such as calcium. Therefore there is a motivation to use calcium since Hanes teaches the particles may be formed with the polymers taught in Cohen et al. Furthermore, Hanes teaches that the formation of the particles may be done by any method known in the art such as Cohen's complex coacervation process.

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913, cited prior art) in view of Cohen et al (5149543) in further view of Yen (5308620).

As set forth above, Hanes et al teach dry powder inhaler compositions. Hanes teaches several active agents including antibiotics in the composition. Cohen et al teach the use of calcium to make a polymer microcapsule.

The references do not specify the pore size.

Yen teaches the method of making stable, porous nanomatrixes. Yen teaches the advantages the porous nature of a carrier vesicle such as this structure allows the

substrate of the biologically active molecules to diffuse into the interior of the nanomatrix and for the reaction products to diffuse out. The drugs can also diffuse out of the nanomatrix at rates dependent on the porosity of the nanomatrix carrier. (Note col. 8, lines 34-46).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hanes et al, Cohen et al, and Yen et al and use instant pore size. One would be motivated to manipulate the pore size is to control the rate of the release of actives from the carrier as taught by Yen; therefore depending on the drug used and the desired rate of release, one would be motivated to manipulate its size.

Response to Arguments

Applicant argues that Yen relates to methods of making protein nanomatrices and intended for injection and not inhalation.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points out that Yen is solely relied upon for pore size and the general reason to manipulate pore size in microspheres, not for the intended use, i.e. inhalation versus intravenous. The motivation to manipulate the pore size and use the instant pore size is provided by Yen's teachings that drugs can diffuse out of the nanomatrix at rates dependent on the porosity of the nanomatrix carrier.

Claim 51 under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913) in view of Cohen et al (5149543) in further view of Igarashi et al (4201774).

As set forth above, Hanes et al teach dry powder inhaler compositions. Hanes teaches several active agents including antibiotics in the composition.

Hanes does not teach the specific use of aminoglycoside antibiotic.

Igarashi et al teaches aminoglycoside antibiotics for the treatment of gram-positive and gram-negative bacteria. Further, the reference teaches the use diluents such as calcium carbonate for the composition and the composition in a form of an inhalant (col. 5, lines19-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the instant medicament in Hanes et al's composition. One would be motivated to do so since the instant antibiotics treat gram-positive and gram-negative bacteria and depending on the patient's requirement, the appropriate drug is used.

Response to Arguments

Applicant does not specifically address the instant rejection therefore the rejection is maintained.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308-2927. The fax phone numbers

for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SSG
July 16, 2003

MICHAEL G. HARTLEY
PRIMARY EXAMINER